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EXAMINER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte GRIGORIY S. TCHAGA and GEORGE G. JOKHADZE

Appeal 2008-3444
Application 10/762,588
Technology Center 1600

Decided: July 23, 2008

Before DONALD E. ADAMS, DEMETRA J. MILLS, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims 11-13, 16, 18-21, and 23-24, the only claims pending in this application. We have jurisdiction under 35 U.S.C. § 6(b).

INTRODUCTION

The claims are directed to a kit for purifying a protein. Claims 11 and 18 are illustrative:

11. A kit for purifying a protein, said kit comprising:
a first composition comprising a first metal ion chelate resin comprising a first immobilized metal ion;
a second composition comprising a second metal ion chelate resin comprising a second immobilized metal ion; and
a recombinant vector comprising a nucleotide sequence encoding a metal ion affinity peptide and at least one restriction endonuclease recognition sequence for inserting a heterologous nucleic acid molecule encoding a fusion partner protein for said metal ion affinity peptide.

18. A kit for purifying a protein, said kit comprising:
a first composition comprising a first metal ion chelate resin comprising a first immobilized Co^{2+} metal ion;
a second composition comprising a second metal ion chelate resin comprising a second immobilized metal ion; and
a recombinant vector comprising a nucleotide sequence encoding a metal ion affinity peptide and at least one restriction endonuclease recognition sequence for inserting a heterologous nucleic acid molecule encoding a fusion partner protein for said metal ion affinity peptide.

The Examiner relies on the following prior art references to show unpatentability:

Tchaga et al.

WO 99/57992

Nov. 18, 1999

Jerker Porath & Birgit Olin, *Immobilized Metal Ion Affinity Adsorption and Immobilized Metal Ion Affinity Chromatography of Biomaterials. Serum Protein Affinities for Gel-Immobilized Iron and Nickel Ions*, 22 Biochemistry 1621-1630 (1983).

The rejection as presented by the Examiner is as follows:

Claims 11-13, 16, 18-21, and 23-24 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Tchaga and Porath.

We affirm.

FINDINGS OF FACT (FF)

1. Tchaga teaches “introducing metal ion affinity sequences into recombinant proteins to allow for purification and/or immobilization of these proteins” (Tchaga Abstract).

2. Tchaga teaches “a recombinant vector comprising an expression vector and a DNA sequence coding for a fusion protein comprising a protein of interest fused . . . to at least one affinity peptide” (Tchaga 4: 24-29).

3. Tchaga teaches that the expression vector contains “unique restriction sites” (Tchaga 6: 2-3; Fig. 1).

4. Tchaga teaches that

[t]he affinity peptide is a histidine-rich polypeptide sequence with a general sequence: $(HX_n)_m$, wherein H is histidine, X is an amino acid other than histidine, $n=1-8$, $m=2-30$, and wherein if $n=1$ for more than two adjacent units of HX, at least one X must be asparagine, phenylalanine, tryptophan, tyrosine, lysine, methionine, arginine, glutamine, or cysteine. The affinity peptide is linked to the proteins of interest R1 and R2 to yield a fusion protein with formula $R1-(HX_n)_m-R2$.

(Tchaga 3: 23 - 4: 3.)

5. Tchaga teaches that “[t]he affinity of the high affinity peptide is for immobilized metal ions” (Tchaga 7: 1-2).

6. Tchaga teaches that “the term ‘protein of interest’ shall refer to any protein to which the affinity peptide is fused for the purpose of purification or immobilization” (Tchaga 8: 23-25).

7. Tchaga teaches

a method for purifying the novel fusion proteins of the present invention, comprising the steps of: contacting a protein sample containing the fusion protein in a mixture with other proteins with a metal chelate resin under conditions where the fusion protein binds to the resin to produce a resin-fusion protein complex.

(Tchaga 5: 9-14.) In this regard, Tchaga exemplifies the purification of proteins of interest on two different metal ion chelate resins (Tchaga 11: 17 - 12: 28 and 14: 12 - 15: 18).

8. Tchaga teaches that “the term ‘metal ion’ refers to any metal ion for which the affinity peptide has affinity and that can be used for purification or immobilization of a fusion protein. Such metal ions include Ni^{+2} , Co^{+2} , Zn^{+2} , Cu^{+2} , Ac^{+3} and Fe^{+3} ” (Tchaga 9: 21-24).

9. Tchaga teaches the metal ion chelate resins “Ni(II)-chelating sepharose FF” (Tchaga 11: 17-18) and Co^{2+} -TALON agarose (Tchaga 14: 12).

10. Porath teaches Ni^{+2} and Fe^{+3} metal ion chelate resins (Porath 1622: col. 2, ll. 27-37).

11. Porath teaches that “[i]n all experiments, each chelator gel was packed in a separate column” (Porath 1622: col. 2, ll. 38-39).

12. Porath teaches an experiment wherein “[t]wo or more columns packed with one type of chelator gel . . . and loaded with different metal ions

were connected in series to form ‘tandem columns’” (Porath 1622: col. 2, ll. 66-69).

13. Appellants’ Specification defines Fe^{3+} as a hard metal ion; and Ni^{2+} and Co^{2+} as an intermediate metal ions (Spec. ¶ 0005).

DISCUSSION

Appellants present the following six groups of claims for our consideration: I. claims 11, 16, and 23; II. claim 12; III. claim 13; IV. claims 18, 21, and 24; V. claim 19; and VI. claim 20. Accordingly, we limit our discussion to claims 11-13 and 18-20. 37 C.F.R. § 41.37(c)(1)(vii).

Tchaga teaches a first composition comprising a first metal ion chelate resin comprising a first immobilized metal ion and a second composition comprising a second metal ion chelate resin comprising a second immobilized metal ion (FF 8 and 9). Tchaga teaches a recombinant vector comprising a nucleotide sequence encoding a metal ion affinity peptide and at least one restriction endonuclease recognition sequence for inserting a heterologous nucleic acid molecule encoding a fusion partner protein for said metal ion affinity peptide (FF 1-6). Both Tchaga and Porath describe the use of metal ion chelate resins to purify a protein of interest (FF 7 and 10-12).

Accordingly, we find no error in the Examiner’s prima facie case, wherein the elements taught by Tchaga are combined into a kit for purifying a protein as taught by both Tchaga and Porath.

Claim 11:

According to Appellants “the methods of Tchaga and Porath address two distinct problems” (App. Br. 9). Therefore, Appellants assert that a person of ordinary skill in this art would “find no reason to combine the teachings of Tchaga . . . with those of Porath . . . since there is no reason to expect that a *method* directed to the purification of untagged proteins would provide an improvement in the purification of ion binding peptide-tagged proteins” (*id.* (emphasis added)). Stated differently,

[t]he references cited teach two strategies for protein purification, one of which relies upon intrinsic affinity of holoproteins for divalent cations and one of which relies overwhelmingly upon the affinity of a designed tag sequence which dominates the interaction of a protein with divalent cations. One of skill therefore would envision no reason to apply the method of the first to the proteins of the second.

(App. Br. 12.)

We are not persuaded. Appellants appear to have lost sight of what they have claimed. Claim 11 is drawn to a kit – not a method.

Appellants do not dispute, and therefore concede, that each of the elements of the kit are taught by the combination of Tchaga and Porath. In addition, Appellants do not dispute, and therefore concede, that it would have been *prima facie* obvious to package the first and second metal ion chelate resins, and the recombinant vector taught by Tchaga into a kit.

There is no requirement in claim 11 that the components of the kit are utilized in a particular manner or that practitioners utilize all the components of the kit. However, Appellants’ do recognize that those of ordinary skill in this art know how to use the components of the kit as taught by Tchaga and Porath to purify a protein (*see e.g.*, App. Br. 12).

Assuming, *arguendo*, that Tchaga and Porath teach divergent methodology for the use of a first and second metal ion chelate resin, this argument does not address the issue of whether it would have been prima facie obvious to package each of the components taught by Tchaga and Porath into a kit to provide a practitioner with metal ion chelate resins and a vector to express metal binding fusion proteins for use in whatever manner the practitioner sees fit.

Accordingly, we affirm the rejection of claim 11 under 35 U.S.C § 103(a) as unpatentable over the combination of Tchaga and Porath. Claims 16 and 23 fall together with claim 11.

Claim 12:

According to Appellants Tchaga and Porath “fail to teach or suggest the use of a tandem pair of columns with specific characteristics of Claim 12 for the purpose of purifying an ion-binding tagged protein” (App. Br. 13). Since claim 12 does not require the components of the kit to be used in any particular manner, we are not persuaded by Appellants’ argument.

Claim 12 depends from and further limits claim 11 to require the first metal ion to be a hard metal ion and the second metal ion to be an intermediate metal ion. Appellants’ Specification defines Fe^{3+} as a hard metal ion; and Ni^{2+} and Co^{2+} as an intermediate metal ions (FF 13).

Tchaga teaches that “[t]he term ‘metal ion’ refers to any metal ion for which the affinity peptide has affinity and that can be used for purification or immobilization of a fusion protein. Such metal ions include Ni^{+2} , Co^{+2} , Zn^{+2} , Cu^{+2} , Ac^{+3} and Fe^{+3} ” (FF 8). More specifically, Tchaga specifically exemplifies the use of Ni^{+2} and Co^{+2} metal ion chelate resins (FF 9). Porath

teaches Ni^{+2} and Fe^{+3} metal ion chelate resins (FF 10). Both Tchaga and Porath teach that the metal ion chelate resins are for purifying proteins.

Appellants have not explained why it would *not* have been prima facie obvious to one of ordinary skill in the art to package any or all of the Ni^{+2} , Co^{+2} , Zn^{+2} , Cu^{+2} , Ac^{+3} and Fe^{+3} metal ion chelate resins into kit form for purifying a protein as taught by Tchaga, or more minimally, the Ni^{+2} , Co^{+2} , and Fe^{+3} metal ion chelate resins exemplified by Tchaga and Porath to be useful in purifying a protein. There is no requirement in claim 12 that the kit be used in any particular manner, accordingly, packaging Ni^{+2} , Co^{+2} , and Fe^{+3} metal ion chelate resins together with a recombinant vector as taught by Tchaga would permit a person of ordinary skill in this art to purify a protein according to either Tchaga's or Porath's methodology.

Accordingly, we affirm the rejection of claim 12 under 35 U.S.C § 103(a) as unpatentable over the combination of Tchaga and Porath.

Claim 13:

Claim 13 depends from and further limits claim 12 to require that the hard metal ion is chosen from Fe^{3+} , Ca^{2+} and Al^{3+} ; and the intermediate metal ion is chosen from Cu^{2+} , Ni^{2+} , Zn^{2+} and Co^{2+} .

According to Appellants

since the instant claim is directed to a kit for purifying an ion-affinity tagged protein which includes metal ion chelate resins in which the first metal ion is a hard metal ion chosen from Fe^{3+} , Ca^{2+} and Al^{3+} , and the second metal ion is an intermediate metal ion chosen from Cu^{2+} , Ni^{2+} , Zn^{2+} and Co^{2+} , the combined references fail to teach or suggest each and every element of Claim 13.

(App. Br. 14.) For the reasons set forth with regard to claim 12 we are not persuaded.

Accordingly, we affirm the rejection of claim 13 under 35 U.S.C § 103(a) as unpatentable over the combination of Tchaga and Porath.

Claim 18:

Appellants rely on their arguments as set forth with regard to claim 1. We are not persuaded for the reasons set forth with regard to claim 1. Regarding the requirement in claim 18 that the first composition comprise a first metal ion chelate resin comprising a first immobilized Co^{2+} metal ion, we note that Tchaga teaches a Co^{2+} metal ion chelate resin and therefore find that it would have been prima facie obvious to include such a resin in a kit for the reasons set forth with regard to claims 12 and 13.

Accordingly, we affirm the rejection of claim 18 under 35 U.S.C § 103(a) as unpatentable over the combination of Tchaga and Porath. Claims 21 and 24 fall together with claim 18.

Claim 19:

Claim 19 depends from and further limits claim 18 to require that the second metal ion is a hard metal ion.

According to Appellants Tchaga is silent with regard to a second column that may be used in a tandem column as taught by Porath and Porath fails to teach the use of Co^{2+} (App. Br. 15). Accordingly, Appellants assert that “the combined references fail to teach or suggest each and every element of the instant Claim 19” (App. Br. 16). We are not persuaded for the reasons set forth with regard to claims 1, 12, and 18.

Accordingly, we affirm the rejection of claim 19 under 35 U.S.C § 103(a) as unpatentable over the combination of Tchaga and Porath.

Claim 20:

Claim 20 depends from and further limits claim 19 to require that the hard metal ion is chosen from Fe^{3+} , Ca^{2+} and Al^{3+} .

According to Appellants Tchaga is silent with regard to a second column that may be used in a tandem column as taught by Porath and Porath fails to teach the use of Co^{2+} , Fe^{3+} , Ca^{2+} and Al^{3+} (App. Br. 16).

Accordingly, Appellants assert that “the combined references fail to teach or suggest each and every element of the instant claim” (*id.*). We are not persuaded for the reasons set forth with regard to claims 1, 12, 13, and 18.

Accordingly, we affirm the rejection of claim 20 under 35 U.S.C § 103(a) as unpatentable over the combination of Tchaga and Porath.

CONCLUSION

In summary, we affirm the rejection of record.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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